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10/585,985	07/13/2006	Naoyuki Kohno	060517	1712

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EXAMINER	
LUM, LEON YUN BON	
ART UNIT	**PAPER NUMBER**
1641	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,985	KOHNO ET AL.	
	Examiner	Art Unit	
	Leon Y. Lum	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *12-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/30/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 1 has been amended to recite a "filtrating" step. This limitation is not, however, recited in the specification. Indeed, different permutations of the term, e.g. filtrate, filtration, are not disclosed in the specification. Accordingly, the specification does not provide literal support for the added limitation. Moreover, the specification does not indicate what type of technique comprises a filtrating step. In the response filed March 30, 2009, Applicants traverse the cited prior art by stating, "[t]he procedure of "filtrating a sample" does not include the meaning of simply "be placed on a sample," thus the two methods are functionally distinct…" Response p.8. Applicants do not, however, explain how "filtrating a sample" as claimed differs from mere placement on a sample either in the response or in the specification. Accordingly, because the

specification does not support a filtrating step either literally or by suggestion, the added limitation is considered new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishibu *et al.*, Analytical Biochemistry (2003) 319:88-95 ("Nishibu").

i. Independent claim 1 is anticipated

Nishibu teaches a method of blotting proteins onto a polyvinylidene difluoride (PVDF) membrane, comprising the steps of (1) mixing a protein solution with ethanol, TCA and SDS to produce a sample and (2) placing the sample in a vacuum pump attached to a PVDF membrane, thereby allowing the protein to become immobilized onto the membrane. *See* page 89, left column second paragraph spanning to the right column, second paragraph. Since Nishibu teaches ethanol, TCA and SDS, the reference teaches the claimed "lower alcohol, and a halogenocarboxylic acid and/or a long chain alkyl sulfate," as claimed. Moreover, the PVDF membrane teaches the claimed "solid-phase having hydrophobic surface." Accordingly, Nishibu teaches all of the claimed elements presented in claim 1.

ii. Dependent claims 2-11 are anticipated

Claims 2-11 are dependent on claim 1 and anticipated by Nishibu for the following reasons.

Regarding claims 2-5, Nishibu teaches ethanol, TCA and SDS. *See supra* rejection of claim 1.

Regarding claims 6-8 and 10-11, Nishibu teaches that the blotting solution can contain 2-5% TCA, 30-50% ethanol and 0.1-0.4% SDS. *See* page 89, right column, second paragraph. Accordingly, claims 6-8 and 10-11 are anticipated for all of the foregoing reasons, including the reason directed at base claim 1 above.

Regarding claim 9, Nishibu teaches that the proteins are blotted onto PVDF. *See supra* rejection of claim 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheley *et al.*, Biotechniques (1991) 10(6):731-732 ("Cheley"), cited in the IDS filed July 22, 2008, in view of Jacobson, Electrophoresis (1990) 11:46-52, cited in the IDS filed July 13, 2006.

i. Independent claim 1 is obvious

Cheley describes a method of immobilizing protein samples to a nitrocellulose membrane using a dot blotter, in which the samples are mixed with a solution of SDS and TCA. Cheley, p.731 (right column, third paragraph). The skilled artisan would recognize that SDS and TCA are, respectively, species of a halogenocarboxylic acid and a long chain alkyl sulfate. Accordingly, Cheley teaches "contacting the protein with the solid-phase" in the presence of "a halogenocarboxylic acid" and "a long chain alkyl sulfate," as claimed. Moreover, because the proteins are being blotted onto a nitrocellulose membrane, they are being selectively transferred onto the membrane

from a different source. *Id.* Accordingly, the proteins are considered to be "filtered." This interpretation is supported by the ordinary and plain meaning of the term "filter," which is defined as "remove by means of a filter." Merriam-Webster OnLine, available at http://www.merriam-webster.com/dictionary/filter[2] (last accessed on July 3, 2009). Here, the proteins are being removed by the nitrocellulose membrane after being mixed with numerous reagents, albeit immobilized on the membrane, Cheley at p.732, with the reagents presumably passing through the membrane. The specification does not contradict this interpretation because, as indicated in the new matter rejection above, a filtering step is neither described nor suggested. Accordingly, Cheley teaches the claimed "filtering" step.

Although Cheley teaches a solid-phase, the reference does not teach that the solid-phase has a hydrophobic surface. Cheley also does not teach that a lower alcohol is included with the halogenocarboxylic acid and long chain alkyl sulfate.

Jacobson descrubes an electrophoretic transfer method that uses a transfer buffer comprising methanol and SDS to transfer proteins from a gel to various types of membranes. Jacobson, p.47 (left column, first paragraph). The membranes include nitrocellulose, nylon and PVDF. *Id*. (right column, third paragraph). Methanol is a well-known lower alcohol and PVDF is a well-known hydrophobic material, as evidenced by Applicants' specification on pages 9-10, paragraph 0022; and page 11, paragraph 0029. Although Jacobson teaches that the PDVF membrane does not provide the most effective protein binding out of all the membranes tested, the PVDF membrane provides high mechanical strength, which is an advantage when colloidal gold and India Ink are

used for staining the proteins. *Id.* at p.50 (right column, first paragraph). Moreover, Jacobson teaches that methanol improves protein binding efficiency. *Id.* at p.47 (right column, second paragraph); p.49 (right column).

With the foregoing description in mind, one of ordinary skill in the art would have found it obvious to modify Cheley's method to include a PVDF membrane and methanol in the transfer buffer. The skilled artisan would have been motivated to perform the modification based on Jacobson's teaching that a PDVF membrane provides high mechanical strength for specific labeling techniques and methanol increases the likelihood of protein binding. Although Jacobson describes methanol's effectiveness in terms of nitrocellulose, the skilled artisan would have found it obvious to apply methanol to the PVDF membrane. Indeed, since PVDF does not provide as effective a binding efficiency as the other membranes tested, the skilled artisan would have attempted to use methanol on PVDF, given it's penchant for improving protein binding on other membrane materials.

ii. Dependent claims 2-5 and 8-10 are obvious

Claims 2-5 and 8-10 are dependent on claim 1 and obvious over the prior art for the following reasons.

Regarding claims 2-5 and 10, Cheley teaches TCA and SDS and Jacobson teaches methanol. *See supra* rejection of claim 1.

Regarding claim 8, Jacobson teaches that the SDS is in a concentration of 0.1%. Jacobson at p.47 (left column first paragraph).

Regarding claim 9, Jacobson teaches that the membrane is PVDF. *See supra* rejection of claim 1.

Claims 6-7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cheley in view of Jacobson, as applied to claim 1.

Regarding claim 11, Jacobson teaches that the SDS is in a concentration of 0.1% and that the membrane is PDVF. Jacobson at p.47 (left column first paragraph and right column, third paragraph).

Cheley and Jacobson, however, do not teach the specifically claimed percentages directed to methanol (claims 6 and 11) and halogenocarboxylic acid (claims 7 and 11).

With the foregoing description, one of ordinary skill in the art would have found it obvious to modify Cheley's TCA and Jacobson's methanol by optimizing the percentages of these compounds to arrive at the claimed ranges. The optimization principle is supported by the *Aller* case, which held that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (CCPA 1955); *see also* MPEP 2144.05. In *Aller*, the claimed process recited a range of temperatures and a range of acid concentrations. *Id*. The court held the process obvious over a reference process that recited the same steps as claimed, but a temperature and acid concentration outside the claimed range. *Id*. Here, the general conditions of the transfer buffer are taught by Cheley and Jacobson, together describing

methanol and TCA and thereby teaching the claimed "lower alcohol" and "halogenocarboxylic acid." Although methanol and TCA are described as being in a percentage outside of the claimed percentage ranges, the skilled artisan, following *Aller* and using routine experimentation, would have found it obvious to modify the percentages disclosed in Cheley and Jacobson to arrive at the claimed ranges.

Response to Arguments

I. Rejection under 35 U.S.C. 102(b) and Rule 132 Declaration

Applicants filed a Rule 132 Declaration in support of their argument that the Nishibu reference is not "by another" as directed under MPEP §§ 715.01(c) and 716.10. *See* Response filed March 30, 2009, p.7. Applicants' argument and submission, however, does not overcome the Nishibu reference.

The instant application is a 371 of PCT/JP05/00737, filed January 21, 2005 and claims priority to PCT/JP2004/000504, which was not filed in the United States and is considered to have a foreign filing date. The statutory bar date is therefor January 21, 2005, the filing date of PCT/JP05/00737. *See* MPEP § 201.13 (stating that "the 1 year bar of 35 U.S.C. 102(b) dates from the U.S. filing date and not from the foreign filing date"). Consequently, because the Nishibu reference was published in 2003, it is prior art under 35 U.S.C. 102(b). Although the previous Office Action included a statement under 35 U.S.C. 102(a), this was presented by mistake. However, the rejection was

properly written and addressed under 35 U.S.C. 102(b). *See* Office Action dated November 28, 2008, p.3. Accordingly, the rejection is maintained.

II. Rejection of claims 1-5 and 8-10 under 35 U.S.C. 103(a)

Applicants traverse the rejection of claims 1-5 and 8-10 under 35 U.S.C. 103(a) as being unpatentable over Cheley in view of Jacobson based on a variety of arguments. Response at pp.8-10. These arguments are not convincing for the following reasons.

Applicants argue that Jacobson does not teach a "filtrating" step. *Id.* at p.8. As noted above, however, the "filtrating" step is taught by Cheley, which describes the transfer of protein from a solution onto a nitrocellulose membrane. *See supra* rejection of claim 1. Accordingly, Applicants' argument does not overcome Jacobson as a reference.

Applicants also argue that Cheley does not teach a lower alcohol with a halogenocarboxylic acid and long chain alkyl surface. *Id.* at p.9. The rejection, however, is based on a combination of references – Cheley and Jacobson – where Jacobson is relied upon to teach the lower alcohol. *See supra* rejection of claim 1. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Accordingly, because Jacobson is relied upon to teach the limitation at issue

and Applicants have not presented an argument why Jacobson is lacking as a reference, Applicants' argument traversing only Cheley is not convincing.

Applicants further argue that Jacobson describes a method to "transfer" protein from a gel but not to "immobilize" the protein on a membrane. *Id.* Applicants allege that because Jacobson describes a migration through nitrocellulose to a filter paper, the protein "cannot be immobilized on the membrane well (Figs. 1 to 3) by Jacobson's method." *Id.* at p.10. Contrary to Applicants' allegations, Jacobson clearly teaches an immobilization step. On page 46, Jacobson describes an "immobilizing matrix" to which proteins are transferred from a polyacrylamide gel. Although the immobilization is the result of a protein transfer and some proteins may be eluted through the matrix, other proteins are clearly immobilized. Because the claims do not require 100% immobilization nor preclude immobilization via protein transfer from a gel, Jacobson appropriately teaches the claimed immobilization step.

Applicants finally argue that because Jacobson indicates that SDS is not preferable for binding in nitrocellulose, the skilled artisan would not have motivation to modify Cheley's method with Jacobson. Response at p.10. Jacobson, however, is relied upon in part to teach a PVDF membrane. The combination of Cheley and Jacobson would therefore have PVDF, not nitrocellulose, as the immobilizing membrane. Although PVDF and nitrocellulose are equivalent materials for the same function, Jacboson does not indicate that PVDF in the presence of SDS would cause a decrease in binding like nitrocellulose does. Moreover, Jacobson describes PVDF as a membrane with good mechanical strength and that using methanol would increase

binding. *See supra* rejection of claim 1. Accordingly, even if SDS did reduce binding with a PVDF membrane, the methanol would provide a counter to this decrease and the PVDF's mechanical qualities provide an incentive for using it as a protein substrate. One of ordinary skill in the art would therefore still have a reason to combine Jacobson with Cheley's method.

The rejection of claims 1-5 and 8-10 is therefore maintained.

III. Rejection of claims 6-7 and 11under 35 U.S.C. 103(a)

Applicants traverse the rejection of claims 6-7 and 11 under 35 U.S.C. 103(a) as being unpatentable over Cheley in view of Jacobson. Response at p.11. Applicants traversed this rejection insofar as the rejection against base claim 1. But because Applicants' arguments are not convincing, *see supra* previous section, they do not overcome the rejection against the instant claims.

The rejection of claims 6-7 and 11 is therefore maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2872. The examiner can normally be reached on Monday to Friday (8:30 am to 5:00 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark L. Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon Y. Lum/
Examiner, Art Unit 1641

/Mark L. Shibuya/
Supervisory Patent Examiner, Art Unit 1641